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NEWS 2	JUL 02	LMEDLINE coverage updated
NEWS 3	JUL 02	SCISEARCH enhanced with complete author names
NEWS 4	JUL 02	CHEMCATS accession numbers revised
NEWS 5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 6	JUL 16	CAplus enhanced with French and German abstracts
NEWS 7	JUL 18	CA/CAplus patent coverage enhanced
NEWS 8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9	JUL 30	USGENE now available on STN
NEWS 10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 11	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 12	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 13	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 14	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 15	AUG 27	USPATOLD now available on STN
NEWS 16	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 17	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 18	SEP 13	FORIS renamed to SOFIS
NEWS 19	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 20	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 21	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 22	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 23	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 24	OCT 19	BEILSTEIN updated with new compounds

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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FILE LAST UPDATED: 12 Nov 2007 (20071112/ED)

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=> S ADHESION ASSAY AND (AUTOIMMUNE OR INFLAMMATORY) DISEASE
MISSING OPERATOR AMMATORY) DISEASE
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> S ADHESION ASSAY AND AUTOIMMUNE DISEASE
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        308719 ADHESION
          4485 ADHESIONS
        310002 ADHESION
                    (ADHESION OR ADHESIONS)
        388504 ASSAY
        171917 ASSAYS
        512601 ASSAY
                    (ASSAY OR ASSAYS)
          1511 ADHESION ASSAY
                    (ADHESION(W)ASSAY)
         55187 AUTOIMMUNE
       1005996 DISEASE
        273226 DISEASES
       1127874 DISEASE
                    (DISEASE OR DISEASES)
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        37990 AUTOIMMUNE DISEASE
              (AUTOIMMUNE(W)DISEASE)
L1          18 ADHESION ASSAY AND AUTOIMMUNE DISEASE

=> L1 AND INFLAMMATORY DISEASE
L1 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
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=> S L1 AND INFLAMMATORY DISEASE
       191019 INFLAMMATORY
          347 INFLAMMATORIES
       191126 INFLAMMATORY
              (INFLAMMATORY OR INFLAMMATORIES)
      1005996 DISEASE
       273226 DISEASES
      1127874 DISEASE
              (DISEASE OR DISEASES)
        13406 INFLAMMATORY DISEASE
              (INFLAMMATORY(W)DISEASE)
L2          3 L1 AND INFLAMMATORY DISEASE

=> D IBIB ABS TOT

L2   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2007:410661  CAPLUS  Full-text
DOCUMENT NUMBER:         146:402310
TITLE:                   Preparation of carbamates, particularly
                         N-(pyrimidin-4-yl)-L-(aminocarbonyloxy)phenylalanine
                         derivatives, which inhibit leukocyte adhesion mediated
                         by VLA-4
INVENTOR(S):             Semko, Christopher Michael; Xu, Ying-Zi; Stappenbeck,
                         Frank; Smith, Jenifer Lea; Rossiter, Kassandra Inez;
                         Fukuda, Juri Y.; Konradi, Andrei W.
PATENT ASSIGNEE(S):      Elan Pharmaceuticals, Inc., USA; Wyeth, John, and
                         Brother Ltd.
SOURCE:                  PCT Int. Appl., 190pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2007041324         A1    20070412    WO 2006-US38113         20060928
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
             KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
             MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
             RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     US 2007129390         A1    20070607    US 2006-541205          20060928
```

PRIORITY APPLN. INFO.: US 2005-722355P P 20050929
OTHER SOURCE(S): MARPAT 146:402310
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are phenylalanines I [Ar = (un)substituted (hetero)aryl; Z = (CH2)n; n = 1-4; X = S, O; T = a bond, S, SO, SO2, NH and derivs.; R1 = (un)substituted alk(en/yn)yl, aryl, heterocyclyl, etc.; R2 = H, acyl, alkyl, alkoxy, etc.; or R1TCNR2 = (un)substituted heterocyclyl containing 4-8 ring atoms; R3, R4 = independently H, alkyl, OH and derivs., heteroaryl, etc.; or R3NR4 = (un)substituted heterocyclyl; provided that when one of R3 and R4 = OH, (un)substituted alkoxy, the other of R3 and R4 = H, (un)substituted cyclo/alkyl, (hetero)aryl, heterocyclyl; R5 = H, (un)substituted alkyl; R6 = carboxy, carboxy ester; R7, R8 = H, (un)substituted alkyl; R7NR8 = (un)substituted heterocyclyl; Y = N, CH; with the exception of specified compds.], their pharmaceutically acceptable salts, esters, and prodrugs, which bind to VLA-4. Certain carbamates I also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Thus, II was prepared by a 6-step synthesis starting from nitropyrimidine-carbamate III. α4β1 Integrin adhesion assays were performed. I are useful for treating inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. I are also useful for treating inflammatory brain diseases such as multiple sclerosis.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:410526 CAPLUS Full-text
DOCUMENT NUMBER: 146:402309
TITLE: Preparation of N-(4-pyrimidinyl)amides, particularly N-(carbamoylpyrimidin-4-yl)-L-[[(aminocarbonyloxy)phenylalanines, which inhibit leukocyte adhesion mediated by VLA-4
INVENTOR(S): Semko, Christopher Michael; Xu, Ying-Zi; Stappenbeck, Frank; Smith, Jenifer Lea; Rossiter, Kassandra Inez; Fukuda, Juri Y.; Konradi, Andrei W.
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Wyeth, John, and Brother Ltd.
SOURCE: PCT Int. Appl., 88pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007041270	A1	20070412	WO 2006-US38009	20060928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,				

UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2007142416 A1 20070621 US 2006-529815 20060928
PRIORITY APPLN. INFO.: US 2005-722358P P 20050929
OTHER SOURCE(S): MARPAT 146:402309
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are phenylalanines I [R1 = halo/alkyl, heteroaryl, NR5R6; R5, R6 = independently H, alkyl; or NR5R6 = heterocyclyl; R2 = alk(en/yn)yl; R3, R4 = alkyl; NR3R4 = heterocyclyl], their pharmaceutically acceptable salts, esters, and prodrugs, which bind to VLA-4. Certain phenylalanines I also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Thus, II was prepared in 8 steps using nitropyrimidine-carbamate III, Et iodide and 3-furoyl chloride. α4β1 Integrin adhesion assays were performed. I are useful for treating inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. I are also useful for treating inflammatory brain diseases such as multiple sclerosis.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:543489 CAPLUS Full-text
DOCUMENT NUMBER: 117:143489
TITLE: preparation of substituted urea and related compounds as cell adhesion modulators
INVENTOR(S): McKenzie, Thomas C.; Rishton, Gilbert M.
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9208464	A1	19920529	WO 1991-US8528	19911114

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
PRIORITY APPLN. INFO.: US 1990-613412 A2 19901115
OTHER SOURCE(S): MARPAT 117:143489
AB Substituted urea, thiourea, and guanidino compds., and salts thereof, are useful as cell receptor antagonists for modulating cell adhesion via integrin and/or fibronectin receptors. These compds. are used for diagnosis, treatment, or prevention of cardiovascular and autoimmune diseases or conditions involving cell adhesion. Thus, 3,4-dichlorophenylguanidine was reacted with 3,5-dimethylpyrazolecarboxamidine nitrate to obtain 1-(3,4-dichlorophenyl)biguanide nitrate (I). The IC50 of I was 65μM in a U937 cell fibronectin adhesion assay.

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=> S NEUTROPHIL ASSAY
         49049 NEUTROPHIL
         36408 NEUTROPHILS
         57908 NEUTROPHIL
                   (NEUTROPHIL OR NEUTROPHILS)
        388504 ASSAY
        171917 ASSAYS
        512601 ASSAY
                   (ASSAY OR ASSAYS)
L3           44 NEUTROPHIL ASSAY
                   (NEUTROPHIL(W)ASSAY)

=> S L3 AND AUTOIMMUNE DISEASE
         55187 AUTOIMMUNE
       1005996 DISEASE
        273226 DISEASES
       1127874 DISEASE
                   (DISEASE OR DISEASES)
         37990 AUTOIMMUNE DISEASE
                   (AUTOIMMUNE(W)DISEASE)
L4            0 L3 AND AUTOIMMUNE DISEASE

=> S L3 AND INFLAMMATORY DISEASE
        191019 INFLAMMATORY
           347 INFLAMMATORIES
        191126 INFLAMMATORY
                   (INFLAMMATORY OR INFLAMMATORIES)
       1005996 DISEASE
        273226 DISEASES
       1127874 DISEASE
                   (DISEASE OR DISEASES)
         13406 INFLAMMATORY DISEASE
                   (INFLAMMATORY(W)DISEASE)
L5            0 L3 AND INFLAMMATORY DISEASE

=> D L1 IBIB ABS TOT

L1   ANSWER 1 OF 18  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:1036145  CAPLUS  Full-text
TITLE:                    Sequence recognition of α-LFA-1-derived peptides
                          by ICAM-1 cell receptors: inhibitors of T-cell
                          adhesion
AUTHOR(S):                Yusuf-Makagiansar, Helena; Yakovleva, Tatyana V.;
                          Tejo, Bimo A.; Jones, Karen; Hu, Yongbo; Verkhivker,
                          Gennady M.; Audus, Kenneth L.; Siahaan, Teruna J.
CORPORATE SOURCE:         Department of Pharmaceutical Chemistry, The University
                          of Kansas, Lawrence, KS, 66047, USA
SOURCE:                   Chemical Biology & Drug Design (2007), 70(3), 237-246
                          CODEN: CBDDAL; ISSN: 1747-0277
PUBLISHER:                Blackwell Publishing Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB    Blocking the T-cell adhesion signal from intercellular adhesion mol.-
      1/leukocyte function-associated antigen-1 interactions (Signal-2) can suppress
      the progression of autoimmune diseases (i.e. type-1 diabetes, psoriasis) and
      prevent allograph rejection.  In this study, we determined the active
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region(s) of cLAB.L peptide [cyclo(1,12)-Pen-ITDGEATDSGC] by synthesizing and evaluating the biol. activity of hexapeptides in inhibiting T-cell adhesion. A new heterotypic T-cell adhesion assay was also developed to provide a model for the T-cell adhesion process during lung inflammation. Two hexapeptides, ITDGEA and DGEATD, were found to be more active than the other linear hexapeptides. The cyclic derivative of ITDGEA [i.e. cyclo(1,6) ITDGEA] has similar activity than the parent linear peptide and has lower activity than cLAB.L peptide. Computational-binding expts. were carried out to explain the possible mechanism of binding of these peptides to intercellular adhesion mol.-1. Both ITDGEA and DGEATD bind the same site on intercellular adhesion mol.-1 and they interact with the Gln34 and Gln73 residues on D1 of intercellular adhesion mol.-1. In the future, more potent derivs. of cyclo(1,6)ITDGEA will be designed by utilizing structural and binding studies of the peptide to intercellular adhesion mol.-1. The heterotypic T-cell adhesion to Calu-3 will also be used as another assay to evaluate the selectivity of the designed peptides.

L1 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:923080 CAPLUS Full-text
DOCUMENT NUMBER: 147:446735
TITLE: Structure-function studies of peptides for cell adhesion inhibition: Identification of key residues by alanine mutation and peptide-truncation approach
AUTHOR(S): Li, Cheng; Satyanarayanajois, Seetharama D.
CORPORATE SOURCE: Department of Pharmacy, National University of Singapore, Singapore, 117543, Singapore
SOURCE: Peptides (New York, NY, United States) (2007), 28(8), 1498-1508
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Blockage of the interaction of CD2 with its ligand CD58 is expected to bring out potential therapeutic value for autoimmune diseases and organ transplantation. Three series of peptides (cVL, cIL and cAQ series) were designed from ratCD2 and humanCD2 to modulate CD2-CD58 interaction. To determine the specific segments in parent peptides responsible for inhibitory activity as lead sequence, the authors generated shorter fragments of the parent peptides and evaluated their biol. activity with cell adhesion assay. The structure-activity relation studies indicated that small cyclic peptides derived from CD2 ligand binding epitopes could mimic native β-turn structure, and thus modulate CD2-CD58 interaction.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:591945 CAPLUS Full-text
DOCUMENT NUMBER: 147:31369
TITLE: Preparation of L-phenylalanine derivatives as α5β1 integrin inhibitors for treating especially solid tumors
INVENTOR(S): Kettle, Jason Grant; Barry, Simon Thomas; Rudge, David Alan
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 210pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007060408	A2	20070531	WO 2006-GB4337	20061122
WO 2007060408	A3	20070802		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-739456P P 20051123
OTHER SOURCE(S): MARPAT 147:31369
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the preparation of L-phenylalanine derivs. I [X = O, NH and derivs., S, SO, SO2; Z = (CH2)n; T = (CH2)m; m, n = independently 0-2; R2a, R2b, R2c = independently H, halo, OH, alkyl, alkoxy, or if 2 of R2a, R2b, R2c are attached to the same C, they may form an oxo group; R3a, R3b, R3c, R3d = independently H, halo, alkyl, alkoxy; R4 = H, ar/heteroar/alkyl, (hetero)aryl; R5 = aryl which is ortho-substituted with at least one group selected from alkyl, alkoxy or halo and which is further optionally substituted with 1 or 2 groups], their pharmaceutical acceptable salts, prodrugs and hydrates, as α5β1 integrin inhibitors, their pharmaceutical compns. and their use alone or in combination with another agent for treatment of diseases that have a significant angiogenesis or vascular component such as solid tumors. The invention also relates to compds. that inhibit α5β1 integrin and that exhibit appropriate selectivity profile(s) against other integrins. Thus, a multi-step synthesis starting from N-(tert-butoxycarbonyl)tyrosine Me ester was given for L-phenylalanine derivative II. I inhibited the α5β1 integrin in an in vitro binding assay (IC50 values in the range of 0.01 to 300 μM) and in an in vitro cell adhesion assay (IC50 values in the range of 0.01 to 50 μM).

L1 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2007:591554 CAPLUS Full-text
DOCUMENT NUMBER:	147:31368
TITLE:	Preparation of L-alanine derivatives as α5β1 integrin inhibitors for treating especially solid tumors
INVENTOR(S):	Kettle, Jason Grant
PATENT ASSIGNEE(S):	Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE:	PCT Int. Appl., 120pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007060409	A1	20070531	WO 2006-GB4338	20061122

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-739486P P 20051123
OTHER SOURCE(S): MARPAT 147:31368
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the preparation of L-alanine derivs. I [X = O, NH and derivs., S, SO, SO2; T = (CH2)m; Z = (CH2)n; m, n = independently 0-2; Y = C or N, provided that when the dashed line is a bond, Y = C; R2a, R2b, R2c = independently H, halo, OH, alkyl, alkoxy, or if 2 of R2a, R2b, R2c are attached to the same C, they may form an oxo group; at least one of A1, A2, A3 and A4 = N and the others = C; R3a, R3b, R3c, R3d = independently H, halo, alkyl, alkoxy, or absent when any of A1-A4 = N; R4 = H, ar/heteroar/alkyl, (hetero)aryl; R5 = aryl which is ortho-substituted with at least one group selected from alkyl or halo and which is further optionally substituted with 1 or 2 groups], their pharmaceutical acceptable salts, prodrugs and hydrates, as α5β1 integrin inhibitors, their pharmaceutical compns. and their use alone or in combination with another agent for treatment of diseases that have a significant angiogenesis or vascular component such as solid tumors (no data). The invention is also related to compds. that inhibit α5β1 integrin and that exhibit appropriate selectivity profile(s) against other integrins. Thus, a multi-step synthesis starting from Me N-(tert-butoxycarbonyl)-3-iodo-L-alaninate and 2,5-dibromopyridine was given for L-alanine derivative II. II inhibited the α5β1 integrin in an in vitro binding assay (IC50 = 6.0 μM) and in an in vitro cell adhesion assay (IC50 = 13.2 μM).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:410661 CAPLUS Full-text
DOCUMENT NUMBER: 146:402310
TITLE: Preparation of carbamates, particularly N-(pyrimidin-4-yl)-L-(aminocarbonyloxy)phenylalanine derivatives, which inhibit leukocyte adhesion mediated by VLA-4
INVENTOR(S): Semko, Christopher Michael; Xu, Ying-Zi; Stappenbeck, Frank; Smith, Jenifer Lea; Rossiter, Kassandra Inez; Fukuda, Juri Y.; Konradi, Andrei W.

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Wyeth, John, and Brother Ltd.
SOURCE: PCT Int. Appl., 190pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007041324	A1	20070412	WO 2006-US38113	20060928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007129390	A1	20070607	US 2006-541205	20060928
PRIORITY APPLN. INFO.:			US 2005-722355P P	20050929

OTHER SOURCE(S): MARPAT 146:402310
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are phenylalanines I [Ar = (un)substituted (hetero)aryl; Z = (CH2)n; n = 1-4; X = S, O; T = a bond, S, SO, SO2, NH and derivs.; R1 = (un)substituted alk(en/yn)yl, aryl, heterocyclyl, etc.; R2 = H, acyl, alkyl, alkoxy, etc.; or R1TCNR2 = (un)substituted heterocyclyl containing 4-8 ring atoms; R3, R4 = independently H, alkyl, OH and derivs., heteroaryl, etc.; or R3NR4 = (un)substituted heterocyclyl; provided that when one of R3 and R4 = OH, (un)substituted alkoxy, the other of R3 and R4 = H, (un)substituted cyclo/alkyl, (hetero)aryl, heterocyclyl; R5 = H, (un)substituted alkyl; R6 = carboxy, carboxy ester; R7, R8 = H, (un)substituted alkyl; R7NR8 = (un)substituted heterocyclyl; Y = N, CH; with the exception of specified compds.], their pharmaceutically acceptable salts, esters, and prodrugs, which bind to VLA-4. Certain carbamates I also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Thus, II was prepared by a 6-step synthesis starting from nitropyrimidine-carbamate III. $\alpha 4\beta 1$ Integrin adhesion assays were performed. I are useful for treating inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. I are also useful for treating inflammatory brain diseases such as multiple sclerosis.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:410526 CAPLUS Full-text
DOCUMENT NUMBER: 146:402309

TITLE: Preparation of N-(4-pyrimidinyl)amides, particularly N-(carbamoylpyrimidin-4-yl)-L-[[(aminocarbonyloxy)phenylalanines, which inhibit leukocyte adhesion mediated by VLA-4

INVENTOR(S): Semko, Christopher Michael; Xu, Ying-Zi; Stappenbeck, Frank; Smith, Jenifer Lea; Rossiter, Kassandra Inez; Fukuda, Juri Y.; Konradi, Andrei W.

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Wyeth, John, and Brother Ltd.

SOURCE: PCT Int. Appl., 88pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007041270	A1	20070412	WO 2006-US38009	20060928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007142416	A1	20070621	US 2006-529815	20060928

PRIORITY APPLN. INFO.: US 2005-722358P P 20050929

OTHER SOURCE(S): MARPAT 146:402309

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are phenylalanines I [R1 = halo/alkyl, heteroaryl, NR5R6; R5, R6 = independently H, alkyl; or NR5R6 = heterocyclyl; R2 = alk(en/yn)yl; R3, R4 = alkyl; NR3R4 = heterocyclyl], their pharmaceutically acceptable salts, esters, and prodrugs, which bind to VLA-4. Certain phenylalanines I also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Thus, II was prepared in 8 steps using nitropyrimidine-carbamate III, Et iodide and 3-furoyl chloride. α4β1 Integrin adhesion assays were performed. I are useful for treating inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. I are also useful for treating inflammatory brain diseases such as multiple sclerosis.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:287513 CAPLUS Full-text

DOCUMENT NUMBER: 146:434677

TITLE: Therapeutic effect of all-trans-retinoic acid (at-RA)

on an autoimmune nephritis experimental model: role of the VLA-4 integrin

AUTHOR(S): Escribese, Maria M.; Conde, Elisa; Martin, Ana; Saenz-Morales, David; Sancho, David; Perez de Lema, Guillermo; Lucio-Cazana, Javier; Sanchez-Madrid, Francisco; Garcia-Bermejo, Maria L.; Mampaso, Francisco M.

CORPORATE SOURCE: Department of Pathology, Hospital Ramon y Cajal, Universidad de Alcala, Madrid, Spain

SOURCE: BMC Nephrology (2007), 8, No pp. given
CODEN: BNMEB7; ISSN: 1471-2369
URL: http://www.biomedcentral.com/content/pdf/1471-2369-8-3.pdf

PUBLISHER: BioMed Central Ltd.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Mercuric chloride (HgCl2) induces an autoimmune nephritis in the Brown Norway (BN) rats characterized by anti-glomerular basement membrane antibodies (anti-GBM Ab) deposition, proteinuria and a severe interstitial nephritis, all evident at day 13 of the disease. We assessed the effects of all-trans retinoic acid (at-RA) in this exptl. model. At-RA is a vitamin A metabolite which has shown beneficial effects on several nephropathies, even though no clear targets for at-RA were provided. We separated animals in four different exptl. groups (HgCl2, HgCl2+at-RA, at-RA and vehicle). From each animal we collected, at days 0 and 13, numerous biol. samples: urine, to measure proteinuria by colorimetry; blood to determine VLA-4 expression by flow citometry; renal tissue to study the expression of VCAM-1 by Western blot, the presence of cellular infiltrates by immunohistochem., the IgG deposition by immunofluorescence, and the cytokines expression by RT-PCR. Addnl., adhesion assays to VCAM-1 were performed using K562 α4 transfectant cells. ANOVA tests were used for statistical significance estimation We found that at-RA significantly decreased the serum levels of anti-GBM and consequently its deposition along the glomerular membrane. At-RA markedly reduced proteinuria as well as the number of cellular infiltrates in the renal interstitium, the levels of TNF-α and IL-1β cytokines and VCAM-1 expression in renal tissue. Moreover, we reported here for the first time in an in vivo model that at-RA reduced, to basal levels, the expression of VLA-4 (α4β1) integrin induced by mercury on peripheral blood leukocytes (PBLs). In addition, using K562 α4 stable transfectant cells, we found that at-RA inhibited VLA-4 dependent cell adhesion to VCAM-1. Here we demonstrate a therapeutic effect of at-RA on an autoimmune exptl. nephritis model in rats. We report a significant reduction of the VLA-4 integrin expression on PBLs as well as the inhibition of the VLA4/VCAM1-dependent leukocyte adhesion by at-RA treatment. Thereby we point out the VLA-4 integrin as a target for at-RA in vivo.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1292873 CAPLUS Full-text

DOCUMENT NUMBER: 146:206619

TITLE: Structure-activity relationship studies of a series of peptidomimetic ligands for α4β1 integrin on Jurkat T-leukemia cells

AUTHOR(S): Liu, Ruiwu; Peng, Li; Han, Huijun; Lam, Kit S.

CORPORATE SOURCE: Division of Hematology and Oncology, Department of Internal Medicine, UC Davis Cancer Center, University of California Davis, Sacramento, CA, 95817, USA

SOURCE: Biopolymers (2006), 84(6), 595-604
CODEN: BIPMAA; ISSN: 0006-3525

PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:206619
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB α4β1 Integrin is a therapeutic target for inflammation, autoimmune diseases, and lymphoid cancers. A series of peptidomimetic ligands based on the Nle-D-I motif have been synthesized and their binding affinities (IC50) to activated α4β1 integrin on Jurkat T-leukemia cells were determined using a cell adhesion assay. One of the 51 ligands, peptide I, has an IC50 = 0.6 nM, more than two fold increase of binding affinity than the initial lead compound II. Extensive SAR studies provided important information for further ligand optimization, which has served as a foundation for studies that ultimately led to identification of a potent ligand with an IC50 = 2 pM.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

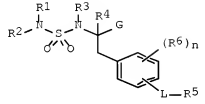
L1 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1107613 CAPLUS Full-text
DOCUMENT NUMBER: 143:326627
TITLE: Preparation of N-(2-phenylethyl)sulfamide derivatives as α4 integrin antagonists for treatment of inflammatory and immune disorders
INVENTOR(S): Jimenez Mayorga, Juan Miguel; Vidal Gispert, Laura; Warrelow, Graham
PATENT ASSIGNEE(S): Almirall Prodesfarma, S.A., Spain
SOURCE: Span., 41 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2219177	A1	20041116	ES 2003-1004	20030505
ES 2219177	B1	20060216		
WO 2004099126	A1	20041118	WO 2004-EP4670	20040503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1622867	A1	20060208	EP 2004-730833	20040503
EP 1622867	B1	20070919		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

CN 1816523	A	20060809	CN 2004-80019205		20040503
JP 2006525271	T	20061109	JP 2006-505356		20040503
AT 373637	T	20071015	AT 2004-730833		20040503
US 2007179183	A1	20070802	US 2006-555286		20061017
PRIORITY APPLN. INFO.:			ES 2003-1004	A	20030505
			WO 2004-EP4670	W	20040503

OTHER SOURCE(S): MARPAT 143:326627

GI



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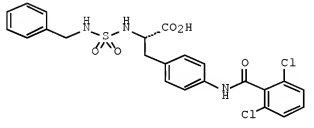


II

AB The invention relates to phenylalanine derivs. I [G = CO2H or tetrazolyl; L = a direct bond, NRc, O, NRcCO, CONRc, O2CNRc, NRcCO2, where Rc = H, alkyl; R1, R2 = independently H, (un)substituted (cyclo)alkyl, alkenyl, alkynyl, heterocyclyl, (hetero)aryl, etc.; or NR1R2 = (un)substituted heterocyclyl, heteroaryl; R3, R4 = H, alkyl; R5 = (un)substituted (hetero)aryl; R6 = OH, alkoxy, NO2, halo, alkylsulfonyl, sulfamoyl, amino, acyl, carboxy, carbamoyl, CN, alkyl, alkenyl, alkynyl, etc.; n = 0-3] and their pharmaceutically-acceptable salts or esters which are α4 integrin antagonists. For example, reaction of Me (2S)-2-[[[(tert- butoxycarbonyl)amino]sulfonyl]amino]-3-[4-[(2,6- dichlorobenzoyl)amino]phenyl]propionate (preparation given) with benzyl alc. in the presence of PBu3 and ADDP in THF, followed by saponification with LiOH•H2O in THF gave (S)-II (43%). In α4β1 adhesion assays, the latter inhibited U-937 cell adhesion to recombinant human soluble VCAM-1 with IC50 values < 100 nM. Thus, I and compns. comprising them are useful for the treatment of inflammatory and immune disorders (no data).

L1 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

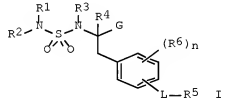
ACCESSION NUMBER:	2004:996111 CAPLUS Full-text
DOCUMENT NUMBER:	141:410709
TITLE:	Preparation of N-(2-phenylethyl)sulfamide derivatives as integrin α4 antagonists for treatment of inflammatory and immune disorders
INVENTOR(S):	Jimenez Mayorga, Juan Miguel; Vidal Gispert, Laura; Warrellow, Graham
PATENT ASSIGNEE(S):	Almirall Prodesfarma, S.A., Spain

SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099126	A1	20041118	WO 2004-EP4670	20040503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2219177	A1	20041116	ES 2003-1004	20030505
ES 2219177	B1	20060216		
EP 1622867	A1	20060208	EP 2004-730833	20040503
EP 1622867	B1	20070919		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1816523	A	20060809	CN 2004-80019205	20040503
JP 2006525271	T	20061109	JP 2006-505356	20040503
US 2007179183	A1	20070802	US 2006-555286	20061017

PRIORITY APPLN. INFO.: ES 2003-1004 A 20030505
WO 2004-EP4670 W 20040503

OTHER SOURCE(S): MARPAT 141:410709
GI



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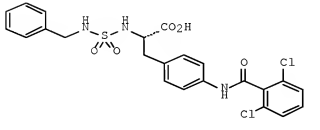


II

AB Title compds. L-phenylalanine derivs. I [wherein G = CO2H, tetrazolyl; L = direct bond, NRc, O, NRcCO, CONRc, OCONRc, NRcCO2; Rc = H, alkyl; R1, R2 = independently H, (un)substituted (cyclo)alkyl, alkenyl, alkynyl, heterocyclyl, (hetero)aryl, etc.; or NR1R2 = (un)substituted heterocyclyl, heteroaryl; R3, R4 = H, alkyl; R5 = (un)substituted (hetero)aryl; R6 = OH, alkoxy, NO2, halo, alkylsulfonyl, sulfamoyl, amino, acyl, carboxy, carbamoyl, CN, alkyl, alkenyl, alkynyl, etc.; n = 0-3; and pharmaceutically acceptable salts and esters thereof] were prepared as integrin α4 antagonists. For example, reaction of Me (2S)-2-[[[(tert-butoxycarbonyl)amino]sulfonyl]amino]-3-[4-[(2,6-dichlorobenzoyl)amino]phenyl]propionate (preparation given) with benzyl alc. in the presence of PBu3 and ADDP in THF, followed by saponification with LiOH•H2O in THF gave (S)-II (43%). In α4β1 adhesion assays, the latter inhibited U-937 cell adhesion to recombinant human soluble VCAM-1 with IC50 values < 100 nM. Thus, I and compns. comprising them are useful for the treatment of inflammatory and immune disorders (no data).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:331928 CAPLUS Full-text

DOCUMENT NUMBER: 140:357354

TITLE: A preparation of benzimidazolone derivatives useful as anti-inflammatory agents

INVENTOR(S): Dhar, T. G. Murali; Potin, Dominique; Maillet, Magali Jeannine Blandine; Launay, Michele; Nicolai, Eric Antoine; Iwanovicz, Edwin J.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004032861	A2	20040422	WO 2003-US31960	20031009
WO 2004032861	A3	20040805		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003282510	A1	20040504	AU 2003-282510	20031009
US 2004116467	A1	20040617	US 2003-681924	20031009
US 6974815	B2	20051213		

PRIORITY APPLN. INFO.: US 2002-417935P P 20021011
WO 2003-US31960 W 20031009

OTHER SOURCE(S): MARPAT 140:357354

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to benzimidazolone derivs. of formula I [wherein: K is O or S; Q is a bond or C(O), etc.; Ar is (un)substituted (hetero)aryl; J1 is a bond, -N(R4)-, etc.; J2 and J3 are -N(R4)- or (un)substituted CH2, etc.; Y and Z are independently selected from N, (un)substituted CH, etc.; R1 = H, (un)substituted alk(en)yl, (hetero)aryl, cycloalkyl, etc.; R2 and R3 are independently selected from H, halogen, NO2, CN, (un)substituted alk(en)yl, etc.; R4 is H, (un)substituted alk(en)yl, CN, C(O)-alkyl, O-alkyl, etc.], their enantiomers, diastereomers, and pharmaceutically- acceptable salts, useful as anti-inflammatory agents. Compds. I were tested in an H1-HeLa adhesion assay and in a HUVEC (human umbilical vein endothelial cells) adhesion assay (no biol. data). For instance, benzimidazole derivative II was prepared via intramol. heterocyclization of the obtained urea derivative III, and N-acetylation of the obtained benzimidazole derivative IV (no yield data).

L1 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:355600 CAPLUS Full-text
DOCUMENT NUMBER: 138:380469
TITLE: SUT-2 and SUT-3 genes, sulfate/anion exchanger polypeptides, and assays for inhibitors of lymphocyte adhesion
INVENTOR(S): Girard, Jean-Philippe; Vincourt, Jean-Baptiste; Amalric, Francois
PATENT ASSIGNEE(S): Fr.
SOURCE: U.S. Pat. Appl. Publ., 160 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003086872	A1	20030508	US 2002-222009	20020814
WO 2003102029	A1	20031211	WO 2002-EP9135	20020814
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002367997	A1	20031219	AU 2002-367997	20020814
EP 1423426	A1	20040602	EP 2002-807483	20020814
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.:		
US 2001-312442P	P	20010815
US 2001-323656P	P	20010919
US 2001-333673P	P	20011126
WO 2002-EP9135	W	20020814

AB The present invention is directed to the SUT-2 and SUT-3 sulfate/anion exchanger polypeptides expressed in high endothelial venules endothelial cells (HEVECs). The invention also relates to drug screening assays for identifying compds. capable of inhibiting sulfate/anion transport and L-selectin mediated lymphocyte adhesion to high endothelial venules. Such compds. are drug candidates for treatment of inflammatory conditions and are claimed for

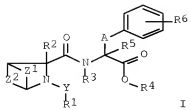
therapeutic uses. CDNAs for two isoforms of human gene SUT-3 protein were cloned from tonsil HEVEC RNA by RT-PCR based on yeast high-affinity sulfate transporter mRNA sequences. SUT-3 protein showed sulfate transporter function when the cDNA was expressed in Sf9 insect cells. A human SUT-3 gene was identified on chromosome 17 and a mouse ortholog on mouse chromosome 11. Human SUT-2 cDNAs were cloned based on sequence homol. with sulfate transporter DTD (diastrophic dysplasia) and SUT-2 genomic sequences were located on human chromosome 8. Functional assays in Xenopus oocytes showed that SUT-2 has activity as a sulfate transporter. Two SUT-2 cDNA isoforms were found to encode the same open reading frame, while another cDNA from kidney was found to encode a second protein isoform with slight modifications in the C-terminus.

L1 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:31445 CAPLUS Full-text
DOCUMENT NUMBER: 136:86057
TITLE: Preparation of aza-bridged-bicyclic amino acid derivatives as α4 integrin antagonists
INVENTOR(S): Dyatkin, Alexey B.; Maryanoff, Bruce E.; Hoekstra, William J.; He, Wei; Kinney, William A.
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002556	A2	20020110	WO 2001-US20857	20010629
WO 2002002556	A3	20020718		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002091115	A1	20020711	US 2001-891602	20010626
US 6960597	B2	20051101		
CA 2415088	A1	20020110	CA 2001-2415088	20010629
EP 1303492	A2	20030423	EP 2001-952331	20010629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012359	A	20030527	BR 2001-12359	20010629
HU 2003001195	A2	20030828	HU 2003-1195	20010629
JP 2004506612	T	20040304	JP 2002-507808	20010629
NZ 523852	A	20041126	NZ 2001-523852	20010629
NO 2002006252	A	20030226	NO 2002-6252	20021227
MX 2003PA00814	A	20041101	MX 2003-PA814	20030127
ZA 2003000794	A	20040429	ZA 2003-794	20030129

PRIORITY APPLN. INFO.:
US 2000-215695P P 20000630
US 2001-891602 A 20010626
WO 2001-US20857 W 20010629

OTHER SOURCE(S): MARPAT 136:86057
GI



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AB Aza-bridged-bicyclic amino acid derivs. I [Y = a bond, CO, CO2, CONH, SO2; R1 = (un)substituted cycloalkyl, heterocyclyl, aryl, haloalkyl, alkyl, alkenyl, alkynyl, heteroaryl; R2, R3, R4 and R5 = H, (un)substituted alkyl, a bond when forming a monocyclic ring; R6 = one to three substituents selected from halogen, alkoxy, (un)substituted cycloalkyl, heterocyclyl, aryl, haloalkyl heteroaryl, amino, arylsulfonyl, etc.; A = (un)substituted alkylene; Z1 and Z2 = (un)substituted alkylene or alkenylene] were prepared as α4β1 and α4β7 integrin receptor antagonists. Thus, condensation of benzenesulfonyl isocyanate with Et glyoxalate, followed by cycloaddn. with cyclohexadiene, hydrogenation, saponification, coupling with (S)-4-nitrophenylalanine Me ester, reduction of the nitro group, acylation with 2,6-dichlorobenzoyl chloride and ester saponification gave 4-[(2,6-dichlorobenzoyl)amino]-N-[[(3S)-2- (phenylsulfonyl)-2-azabicyclo[2.2.2]oct-3-yl]carbonyl]-L-phenylalanine, which showed IC50 = 21nM in Ramos cell adhesion assay.

L1 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:194157 CAPLUS Full-text
DOCUMENT NUMBER: 130:232490
TITLE: Synthetic divalent sLex-containing polylactosamines and their preparation for blocking lymphocyte binding and treatment of inflammatory or other diseases
INVENTOR(S): Renkonen, Ossi; Renkonen, Risto
PATENT ASSIGNEE(S): Glycim Oy, Finland
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9912944	A2	19990318	WO 1998-FI688	19980904
WO 9912944	A3	19990826		
W: AM, AT, AU, AZ, BA, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KG, KR, KZ, LT, LU, LV, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TR, UA, UZ, YU, MD				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2302470	A1	19990318	CA 1998-2302470	19980904
AU 9890739	A	19990329	AU 1998-90739	19980904
EP 1015464	A2	20000705	EP 1998-942706	19980904
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

US 6191271	B1	20010220	US 1998-148076		19980904
HU 2000003418	A2	20010228	HU 2000-3418		19980904
JP 2001515912	T	20010925	JP 2000-510750		19980904
NO 2000001091	A	20000302	NO 2000-1091		20000302
PRIORITY APPLN. INFO.:			US 1997-57660P	P	19970905
			WO 1998-FI688	W	19980904

AB The present invention is directed to novel compns. and their use in the treatment of inflammatory responses. Specifically, the invention is directed to novel synthetic oligosaccharide constructs and their use to block lymphocyte binding to correspondent oligosaccharides on the endothelial surface, and thus reduce or otherwise ameliorate an undesired inflammatory response. The invention is further directed to the use of such constructs in other disease states characterized by selectin binding, such as bacterial infections and metastatic cancers. The divalent sLexLex glycan (preparation given) was the most potent inhibitor of lymphocyte adhesion to high endothelial venules (HEV) in the L-selectin-dependent cell adhesion assay.

L1 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1996:581604 CAPLUS Full-text
DOCUMENT NUMBER:	125:245619
TITLE:	Regulation of sialoadhesin expression on rat macrophages. Induction by glucocorticoids and enhancement by IFN-β, IFN-γ, IL-4, and lipopolysaccharide
AUTHOR(S):	van den Berg, Timo K.; van Die, Irma; de Lavalettte, Chantal Renardel; Doepp, Ed A.; Smit, Larissa D.; van der Meide, Peter H.; Tilders, Fred J. H.; Crocker, Paul R.; Dijkstra, Christine D.
CORPORATE SOURCE:	Medical Fac., Vrije Univ., Amsterdam, Neth.
SOURCE:	Journal of Immunology (1996), 157(7), 3130-3138 CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER:	American Association of Immunologists
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Sialoadhesin is a macrophage-restricted member of the Ig superfamily that mediates adhesion with lymphoid and myeloid cells. It is expressed on a subpopulation of macrophages in lymphoid tissues and in chronic inflammation (e.g., during autoimmune diseases). We have studied the regulation of sialoadhesin expression in vitro and show that glucocorticoids (GC) induce sialoadhesin expression on freshly isolated rat macrophages and the rat macrophage cell line R2. The cytokines IFN-β, IFN-γ, IL-4, and LPS, although unable to induce sialoadhesin expression by themselves, were able to enhance GC-mediated induction of sialoadhesin. Sialoadhesin expression was functional as shown by cell adhesion assays with human RBCs. Northern blotting expts. indicated that regulation predominantly occurred at the mRNA level. Comparison of the different combinations of GC and cytokines/LPS revealed differences in the level of GC-dependent enhancement of sialoadhesin expression, with IFN-β and IL-4 being more potent than IFN-γ and LPS. Moreover, the effects of IFN-γ and LPS could be reproduced by priming, whereas IFN-β and IL-4 were required simultaneously with GC. The regulation of sialoadhesin expression was mediated by the GC receptor, and not by mineralocorticoid receptor, as shown by inhibition expts. with specific antagonists. Finally, it is demonstrated that macrophages in the adrenal gland, the major site of endogenous GC production, express sialoadhesin. This study demonstrates that GC act as a primary inducer of sialoadhesin expression on rat macrophages, and that the response can be enhanced by IFN-β, T cell-derived cytokines, or LPS.

L1 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:821507 CAPLUS Full-text
DOCUMENT NUMBER: 123:225873
TITLE: sLex is not responsible for the interaction of sLex-positive memory T lymphocytes with E-selectin
AUTHOR(S): Rotteveel, F. T. M.; Van Doornmalen, A. M.; Van Duin, M.
CORPORATE SOURCE: Dep. Immunology, NV Organon, Oss, Neth.
SOURCE: Immunology (1995), 86(1), 34-40
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB E-selectin is an adhesion mol. that is transiently and exclusively expressed on endothelial cells in response to inflammatory cytokines. In addition, E-selectin participates in the initial interaction of leukocytes with activated endothelial cells. This role of E-selectin in cell adhesion has made it a potential target for modulation of inflammatory processes that, for example, are occurring in autoimmune diseases such as rheumatoid arthritis. Although on granulocytes the ligand for E-selectin has been identified as the tetrasaccharide sialyl Lewis x (sLex), the mol. nature of this ligand on T lymphocytes has not yet been identified. In the present study, it was shown by fluorescence-activated cell sorter (FACS) anal. with the anti-sLex antibody CSLEX1 that T lymphocytes stimulated with phytohemagglutinin (PHA), interleukin-2 (IL-2), and transforming growth factor-β1 (TGF-β1) expressed sLex. Furthermore, in a cell adhesion assay these activated T cells of the memory phenotype bound specifically to E-selectin-transfected Chinese hamster ovary (E-CHO) cells. This adhesion was blocked with an anti-E-selectin antibody but not with CSLEX1. In the same assay, the interaction of sLex-pos. U937 cells with the E-CHO cells could be inhibited both with anti-E-selectin and CSLEX1 antibodies. Thus, sLex on activated T lymphocytes is not responsible for the interaction with E-selectin. Rather, these results suggest that stimulated T lymphocytes express an addnl. E-selectin ligand(s) with much higher avidity for E-selectin than sLex.

L1 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:331099 CAPLUS Full-text
DOCUMENT NUMBER: 122:96538
TITLE: Heparin-like oligosaccharides for selectin receptor modulating compositions
INVENTOR(S): Bevilacqua, Michael P.; Nelson, Richard M.; Linhardt, Robert J.
PATENT ASSIGNEE(S): Regents of the University of California, USA; University of Iowa Research Foundation
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9426759	A1	19941124	WO 1994-US5327	19940513
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5527785	A	19960618	US 1993-89076	19930707
PRIORITY APPLN. INFO.:			US 1993-62957 A	19930514

US 1993-89076 A 19930707

AB Selectin receptor binding (associated with e.g. inflammation, infection, malignancy, etc.) is modulated by a method which utilizes heparin-like oligosaccharides. Results of in vitro adhesion assays , as well as in vivo effects of heparin fragments, are presented.

L1 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:543489 CAPLUS Full-text
DOCUMENT NUMBER: 117:143489
TITLE: preparation of substituted urea and related compounds as cell adhesion modulators
INVENTOR(S): McKenzie, Thomas C.; Rishton, Gilbert M.
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9208464	A1	19920529	WO 1991-US8528	19911114
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
PRIORITY APPLN. INFO.:			US 1990-613412	A2 19901115
OTHER SOURCE(S):	MARPAT 117:143489			

AB Substituted urea, thiourea, and guanidino compds., and salts thereof, are useful as cell receptor antagonists for modulating cell adhesion via integrin and/or fibronectin receptors. These compds. are used for diagnosis, treatment, or prevention of cardiovascular and autoimmune diseases or conditions involving cell adhesion. Thus, 3,4-dichlorophenylguanidine was reacted with 3,5-dimethylpyrazolecarboxamidine nitrate to obtain 1-(3,4-dichlorophenyl)biguanide nitrate (I). The IC50 of I was 65μM in a U937 cell fibronectin adhesion assay.

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=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	112.22	112.43
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-16.38	-16.38

STN INTERNATIONAL LOGOFF AT 18:56:07 ON 13 NOV 2007